Response

Dear Editors:

We appreciate Dr. Aksoy's response to our paper and the specific data it provides regarding the methodology used in his studies to calculate leukemia incidence and to estimate benzene concentrations to which his cohort of Turkish shoe, slipper, and handbag workers was exposed. It is without question that Dr. Aksoy's early epidemiologic observations of the association between benzene exposure and leukemia are to be commended. The major conclusion of our review, however, was that the Aksoy studies, as well as some of the other available benzene epidemiologic studies, are not optimal for risk assessment, due primarily to limitations in quantitative exposure information. Given that individual exposure history data were not apparently available for workers in the Aksoy study, it remains our judgment that it provides a less useful basis for the estimation of a dose-response relationship than the Rinsky et al. study that we selected.

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Other Factors in Leukemia

Dear Editors:

In their interesting paper "Consistencies and Inconsistencies Underlying the Quantitative Assessment of Leukemia Risk from Benzene Exposure," Lamm et al. (*1*) discussed the results of our paper concerning the distribution of the types of leukemia in chronic benzene toxicity. According to Lamm et al., 43 (84%) of 51 cases of leukemia in my series with chronic benzene toxicity had acute myelocytic leukemia (AML) (*2*). Unfortunately, there is an important mistake in this calculation. As can be seen easily from the paper concerning 51 leukemic shoeworkers with chronic benzene toxicity, only 20 (39.25%) had AML (*2*). The remaining were acute lymphoblastic leukemia, 5 shoeworkers (9.8%); preleukemia, 7 (13.75%); acute erythroleukemia, 10 (19.6%); acute myelomonocytic leukemia, 4 (7.85%); acute monocytic leukemia, 1 (1.95%); acute undifferentiated leukemia, 1 (1.95%); and chronic myeloid leukemia, 2 (3.9%). On the other hand, it is a matter of fact that there are significant differences concerning the distribution of the types of leukemia in several studies on this hematologic malignancy associated with chronic benzene exposure. In one group, acute types of leukemia predominate, as seen in Vigliani and Forni (*3*), Aksoy et al. (*2*), Infante et al. (*4*), and Yin et al. (*5*) series. Contrary to these, in series of Tareef et al. (*6*), Goguel et al. (*7*), and Browning, who collected series from the literature (*8*), chronic types of leukemia take the first place in the series of leukemia due to chronic benzene toxicity. Considering the above-mentioned striking differences, we suggested that these findings may be partly explained by exposure levels, the mode of exposure, and the presence or absence of other homologs of benzene such as toluene and xylene or other chemicals (*9*).

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Response

Dear Editors:

We are pleased to hear from the distinguished Professor Muzaffer Aksoy who has contributed greatly to the literature on benzene and leukemia. He has raised a number of questions concerning our review (*1*) and analysis of the epidemiological studies of benzene and leukemia. In our review, we analyzed the set of published population-based studies of leukemia (case count five or greater) among benzene-exposed workers. We included all the studies that (*a*) indicated the size and definition of the population studied, (*b*) commented on the characteristics of the benzene exposure, and (*c*) appeared to have identified all the cases within their studied population. The second group of studies that

Aksoy mentioned did not meet these criteria. Those studies either reviewed the literature or analyzed case series; each lack both a specific study population (or complete case count) and a measurement of the benzene exposure. Our literature review is complete for the studies that meet the criteria.

Aksoy has questioned our description that 84% of his reported leukemias (*2*) in benzene-exposed workers were acute myeloid leukemias (AML). As discussed in our paper, we used the term "acute myeloid leukemia" to encompass all the variants of acute leukemia of myeloid origin classified by the FAB (French-American-British Cooperative Group) (*3*) as the M_1 through M_7 categories. We thus included in the AML category not only the myeloblastic leukemias but also the erythroleukemias, promyelocytic leukemia, monocytic leukemias, myelo-monocytic leukemias, and would have included megakaryoblastic leukemias if there had been any. We also included the group of preleukemias (myelodysplastic syndrome) which usually terminate as AML, since Aksoy included them in his list of leukemias. Had we not included the preleukemias, we would have reported that 81% (34/42) of the leukemias reported by Aksoy in benzene-exposed workers were AML. The only cases in Aksoy's reports that do not belong in the AML category as defined by the FAB group and described in our paper are the five acute lymphoblastic leukemia cases, the two chronic myelogenous leukemia cases, and (possibly) the undifferentiated leukemia case (where one needs markers of karyotype findings to better ascertain origin).

The observations from Professor Aksoy's study are consistent with the general observation that it is the AMLs that are found in excess among benzene-exposed workers. In 1977, Goldstein (*4*) had reviewed the world's literature which included the studies cited by Aksoy and concluded that only AML and its variants had been definitely associated with benzene exposure. We have now extended that observation to the subsequently published epidemiological literature and have concluded that it is AML that can be caused by excessive benzene exposure. While individual case reports and case series have reported chronic leukemias in benzene-exposed workers, the hypothesis that they are found in excess among benzene—exposed workers is not supported by the data in the epidemiological literature. Some previous studies initially indicating an excess of chronic leukemias among solvent-exposed workers (where benzene had been the solvent of choice) (*5*) have subsequently been found to be related to nonbenzene solvent exposures, such as carbon disulfide and not to benzene (*6*). We concur with Professor Aksoy's suggestion that the other disorders may relate to nonbenzene exposure (*7*).

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